II. REMARKS

Preliminary Remarks

The title and abstract of the application are amended so as to identify the elected invention, as requested in the Office Action.

The first paragraph of the specification is amended to update the status of the priority documents.

Paragraphs of the specification that refer to figures showing sequence information are amended to identify the corresponding SEQ ID NOs, and names of trademarked products are re-written as called for in the Office Action.

Non-elected claims 1-10, 13-18, and 21-26 are canceled without prejudice. Claims 11, 12, 19, 20, and 27-33 are amended, and new claims 34-55 are added.

The claims are amended to use the alternative term CD80 in referring to the B7.1 antigen protein, support for which is found on page 1, line 16. Claim 11 is amended to be directed to a method for inhibiting or preventing T cell/B cell interactions associated with Crohn's disease; and claim 27 is amended to be directed to a method of treating Crohn's disease; support for which is found in the specification, for example, on line 4 of page 46.

Amended claims 11 and 27, and new claims 40-44 and 51-55 are directed to methods in which a CD80-binding fragment of an anti-CD80 antibody is administered, support for which is found, for example, on page 41, lines 16-18, and page 47, lines 10-11.

Amended claims 12, and 28 are directed to methods in which the anti-CD80 antibody is a chimeric antibody comprising variable regions of a non-human anti-CD80 antibody and human constant regions; and amended claims 20 and 29 and new claims 43 and 54 are directed to antibodies having variable regions of an Old World monkey anti-CD80 antibody, support for which is found in the specification, for example, in the description of making Primatized® monoclonal antibodies on pages 38-39, as well as in U.S. Patent No. 5,658,570, which describes making chimeric antibodies having human constant regions and either murine or monkey variable regions (e.g., in columns 1-4) and which is incorporated by reference.

Amended claim 19 and new claims 34-39, 42-50, 54 and 55 are directed to an anti-CD80 antibody that has the same variable regions as, or competes for binding to CD80 with,

antibody 7C10 or antibody 16C10, support for which is found in the specification, for example, on pages 33-36, which describe methods for making anti-CD80 antibodies that were used to obtain the 7C10 and 16C10 antibodies, on pages 38-39, which describe methods for cloning DNA sequences encoding the variable regions of the antibodies and expressing these using vectors containing DNA sequences encoding human constant regions, to produce chimeric, Primatized®antibodies having the variable regions of 7C10 and 16C10; and in Examples 9-11 on pages 68-71, which describe competitive binding assays that identify anti-CD80 antibodies and other CD80-binding proteins that compete for binding to CD80 antigen with 7C10 and 16C10 antibodies.

Amended claims 30 and 32 are directed to administering CD80 antibody in combination with an immunomodulator selected from the group consisting of IL-7, IL-10, CTLA4-Ig, soluble CTLA-4, an anti-CD28 antibody or fragment thereof, support for which is found in the specification, for example, on page 51, lines 3-6.

Amended claims 31 and 33 are directed to administering CD80 antibody in combination with an immunosuppressant selected from the group consisting of cyclosporin A, FK506, anti-TNFα, anti-CD54, anti-CD11, anti-CD11a, anti-IL-1, TNFα receptor, and IL-1 receptor, support for which is found in the specification, for example, on page 51, lines 7-10. Claims 31 and 33 are also amended to correct a typographical error in "FK506."

Patentability Remarks

35 U.S.C. §112, First Paragraph

A. Written description

The amended claims do not refer to "humanized" antibodies, and Applicants respectfully request that the objection to claims 12 and 20 for lack of written description of this term be withdrawn.

Claim 30 is amended by deleting the phrase, "entities that modulate the B7/CD28 pathway" that was ground for rejection for lack of written description. The amended claims are directed to co-administration of an immunomodulator selected from the group consisting of IL-7, IL-10, CTLA4-Ig, soluble CTLA-4, an anti-CD28 antibody or fragment thereof, as

disclosed on page 51, lines 3-6. Accordingly, Applicants respectfully request that the rejection of claims 30 and 31 for lack of written description also be withdrawn.

B. Enablement

Applicants respectfully traverse the rejection of claims 11-12, 19-20, and 27-33 under 35 U.S.C. 112, first paragraph, on the grounds that the specification does not enable one skilled in the art to make or use the claimed invention. As amended, the claims are directed to a method for treating Crohn's disease comprising administering a therapeutically effective amount of an anti-CD80 antibody or antibody fragment that binds specifically to CD80 antigen without inhibiting the binding of CD80 antigen to CTLA-4.

The present application discloses the new discovery that therapeutic antibodies that bind specifically to human CD80 antigen without inhibiting the binding of CD80 antigen to CTLA-4 can be obtained using known methods of molecular biology and cellular immunology as described in the application. The application describes assay methods that persons skilled in the art can use to screen anti-CD80 antibodies produced by the disclosed methods to identify anti-CD80 antibodies that bind specifically to CD80 without inhibiting the binding of CD80 antigen to CTLA-4; and it discloses two working examples of such antibodies, monkey monoclonal antibodies 7C10 and 16C10 (see Examples 3-11). The application further describes making primatized anti-CD80 antibodies that can be administered therapeutically to a human subject without eliciting an antibody-specific immune response, and it discloses the amino acid sequences of the light and heavy chains of two primatized therapeutic antibodies having the variable regions of the 7C10 and 16C10 antibodies, respectively, and human constant regions (see page 33, Figures 3a-3b, and Figures 5a-5b).

People who are skilled in the art of making and using therapeutic monoclonal antibodies have a high level of training and skill, often at the Ph.D. level. Applicants submit that such skilled persons are able to follow the teachings of the present application and use the methods described therein to obtain antibodies that bind specifically to CD80 without inhibiting the binding of CD80 antigen to CTLA-4 without undue experimentation. Applicants further submit that persons skilled in the art are able follow the teachings of the present application and administer a therapeutically effective amount of a monoclonal anti-

CD80 that does not inhibit the CD80/CTLA-4 binding interaction to successfully treat Crohn's disease, also without having to perform undue experimentation. The Applicants therefore respectfully request that the rejection of the claims under 35 U.S.C. 112, first paragraph, for non-enablement, be withdrawn.

35 U.S.C. §112, Second Paragraph

Amended claims 30 and 31 do not use the verb "modulates" that was the basis for rejecting the claims under 35 U.S.C. 112, 2nd paragraph. Withdrawal of the rejection is therefore respectfully requested.

35 U.S.C. §102(e)

Claims 11 and 19 were rejected under 35 U.S.C. §102(e) as being anticipated by Linsley et al. (U.S. Patent No. 5,844,095).

Claims 11-12 and 19-20 were rejected under 35 U.S.C. 103(a) as being obvious in view of the '095 patent of Linsley et al., in combination with Aruffo et al. (U.S. Patent No. 6,051,228).

As amended, all of the claims are directed to methods comprising administering anti-CD80 antibodies or fragments thereof that bind specifically to CD80 without inhibiting the binding of CD80 antigen to CTLA-4. Paragraph 20 of the Office Action acknowledges that methods of administering anti-CD80 antibodies that do not inhibit the CD80/CTLA-4 binding interaction are free of the prior art. The Applicants therefore submit that the claims are neither anticipated by nor obvious in view of the cited references, and respectfully request that the rejection of the claims under 35 U.S.C. 102(e) and 103(a) in view of the prior art be withdrawn.

Conclusion

All rejections having been addressed, it is respectfully submitted that the present application is in condition for allowance and a Notice to that effect is earnestly solicited. If any points remain in issue, which the examiner feels may be best resolved through a personal or telephone interview, he is kindly requested to contact the undersigned attorney at the telephone number listed below.

Respectfully submitted,

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